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BLOOD AS A BIOLOGICAL "DRUG":
SCIENTIFIC, LEGAL, AND POLICY ISSUES IN THE
REGULATION OF PLACENTAL AND UMBILICAL CORD
STEM CELL TRANSPLANTATION

*Jennifer Kulynych**

In Southern California, this is already spreading like crazy—it's becoming cocktail party conversation.¹

[W]ell-intentioned people cry out against a proposal they do not fully understand²

There are a lot of people out there doing bad things, it's scary³

I. INTRODUCTION

Not all blood cells are created equal. Some are born, carry out their appointed tasks—red blood cells oxygenating the blood, white blood cells fighting infection—and die. But an elusive subset have special properties: they are the progenitors of all the many types of peripheral (circulatory) blood cells, and as such, they have the potential to reconstitute an entire blood supply.⁴ Known as *hematopoietic stem cells*, these blood cells

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1. Tim Cady of the Cord Blood Registry, *quoted in* Shari Roan, *From a New Life Can Come the Chance to Save Another*, L.A. TIMES, May 1, 1996, at E1, E2.

2. Letter from Pablo Rubenstein, M.D., New York Blood Center, to the Food and Drug Administration (FDA) 3 (July 12, 1996) (on file with the FDA).

3. Hal Broxmeyer, Indiana University School of Medicine, *quoted in* Susan Cohen, *Tangle Lifeline: The Cord Blood in a Newborn's Placenta Looks to Researchers Like a Fountainhead of New Lifesaving Therapies*, WASH. POST MAG., Aug. 18, 1996, at 10, 28.

4. See Leslie E. Silberstein & Leigh C. Jefferies, *Placental Blood Banking—A New Frontier in Transfusion Medicine*, 335 NEW ENG. J. MED. 199, 200 (1996).

reproduce indefinitely. For patients with leukemia or other blood diseases, the transplantation of hematopoietic stem cells from another person's bone marrow can provide the gift of life.⁵

Unfortunately, harvesting and transplanting bone marrow stem cells is costly and painful for both donor and recipient. Bone marrow transplantation is further complicated by the fact that donor and recipient must be closely matched on a range of immunological factors.⁶ The cost (expenses can exceed \$250,000), pain, and difficult logistics of bone marrow transplantation result in an estimated 50,000 patients per year failing to receive needed transplants.⁷

In 1988, however, a medical breakthrough occurred. Researchers successfully exploited a new source of hematopoietic stem cells when "cord blood"—blood harvested at birth from human placentas and umbilical cords—was used in France to repopulate the blood supply of a child with a rare, lethal form of anemia.⁸ Interest in cord blood transplantation was immediate, because the new technique appeared to have several advantages over bone marrow transplantation: cord blood was readily available, painless to obtain, and a particularly rich source of blood-producing stem cells.⁹ Even better, the relative immaturity of cord blood stem cells offered the possibility that transplant recipients and donors might not need to be so closely matched for immunological factors, thus greatly expanding the range of patients who might benefit from transplantation.¹⁰

As the scientific investigation of cord blood progressed, enthusiastic researchers soon came into contact with venture capitalists, and a new form of biotech entrepreneurship was born: the

5. See *id.*

6. These immunological factors are known as HLA antigens. See discussion *infra* Part II.A.

7. See Ron Winslow, *Placenta May Be Source of Cells Vital in Bone Marrow Transplants*, WALL ST. J., Nov. 12, 1992, at B6.

8. See E. Gluckman et al., *Hematopoietic Reconstitution in a Patient with Fanconi's Anemia by Means of Umbilical-Cord Blood from an HLA-Identical Sibling*, 321 NEW ENG. J. MED. 1174, 1174 (1989).

9. See Cohen, *supra* note 3, at 11-12.

10. See Silberstein & Jefferies, *supra* note 4, at 199; see generally Hal Broxmeyer, *Questions to be Answered Regarding Umbilical Cord Blood Hematopoietic Stem and Progenitor Cells and Their Use in Transplantation*, 35 TRANSFUSION 694 (1995).

for-profit cord blood bank.¹¹ The target market for commercial cord blood services was vast, potentially including every expectant parent in the United States. With amazing rapidity, what has been termed a "biological gold rush" had begun.¹²

From the date of the first successful transplant in 1988, cord blood studies have yielded promising results in the treatment of childhood leukemia and hereditary blood and immune diseases.¹³ However, manipulative cord blood marketing techniques and some researchers' safety concerns soon prompted complaints to the Food and Drug Administration (FDA). In response, the FDA has proposed to enter the cord blood field as a regulator.¹⁴ After holding workshops on the issue, the FDA released a draft document outlining a possible regulatory approach to cord blood transplantation;¹⁵ this tentative step generated heated controversy among scientists and among participants in the private cord blood banking industry. A campaign of newspaper editorials and letters to congressmen ensued, many written by panicked parents who were convinced that FDA regulation would destroy the seemingly magical potential of cord blood banking.¹⁶

Inevitably, public outcry and industry lobbying brought political scrutiny to the regulatory process, and cord blood transplantation became a set piece in the FDA regulatory reform cam-

11. See Cohen, *supra* note 3, at 14-15.

12. See *id.* at 13 ("There is already competition in the delivery suite, like a rush for biological gold.")

13. See Silberstein & Jefferies, *supra* note 4, at 200.

14. Telephone Interview with Liana Harvath, Ph.D., Chief, Lab of Cellular Hematology, FDA (Dec. 2, 1996); see also Letter from Diane E. Thompson, Associate FDA Commissioner for Legislative Affairs, to the Honorable Robert E. Andrews, United States House of Representatives 1 (July 31, 1996) (on file with the FDA).

15. See CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, DRAFT DOCUMENT CONCERNING THE REGULATION OF PLACENTAL/UMBILICAL CORD BLOOD STEM CELL PRODUCTS INTENDED FOR TRANSPLANTATION OR FURTHER MANUFACTURE INTO INJECTABLE PRODUCTS (FDA Docket No. 96N-0002), Feb. 26, 1996 [hereinafter CORD BLOOD DRAFT DOCUMENT].

16. See, e.g., Linda DeSpain, *The FDA Snuffs a Ray of Hope*, WALL ST. J., June 18, 1996, at A22; *Parents Fear Blood Bank Rules: FDA Blames Cord-Blood Panic on 'Misinformation' by Banks*, RICH. TIMES-DISPATCH, June 16, 1996, at A2 (hereinafter *Parents Fear Rules*).

The FDA has 16 volumes of cord blood public commentary on file and available for public inspection at the Documents Management Branch (HFA-305), Food and Drug Administration, Rm. 1-23, 12420 Parklawn Dr., Rockville, Maryland 20857.

paign that swept through the 104th Congress.¹⁷ Senator Ron Wyden (D-Oregon) introduced the Human Tissue Safety Act of 1996,¹⁸ a bill that would, *inter alia*, specifically exempt cord blood from most aspects of the FDA's regulatory oversight.¹⁹ The 1996 Tissue Act failed to emerge from committee, but because FDA reform remains high on the agenda of the new Congress, similar provisions regarding cord blood may be incorporated into FDA reform legislation in the 105th Congress. Meanwhile, in February of 1997, the FDA issued a comprehensive draft proposal for the regulation of all human tissue, with provisions specific to cord blood stem cells.²⁰ These provisions modify the FDA's earlier, more cautious approach to cord blood regulation.

This article will examine the controversy over cord blood regulation. Part II provides background information on cord blood transplantation and describes the two regulatory approaches that the FDA has proposed to date. Part III surveys unresolved scientific questions about cord blood transplantation, while Part IV examines policy arguments for and against cord blood regulation and explores the difficult questions of property law that arise when cord blood is treated as a marketable commodity. Part V describes the Tissue Act and its intended consequences. The article concludes that the Tissue Act is a conceptually flawed solution to the cord blood controversy, and further, that as a result of the passage of this or a similar bill, careful consideration of the many unresolved ethical and scientific issues involved in cord blood transplantation would be cut short by a legislative fiat. Rather than capitulating to political and industry pressure and adopting weakened regulatory requirements, the FDA should proceed with its original, scien-

17. See Charles A. Walsh & Alissa Pyrich, *Rationalizing the Regulation of Prescription Drugs and Medical Devices: Perspectives on Private Certification and Tort Reform*, 48 RUTGERS L. REV. 883, 886 (1996) (discussing FDA as a target of regulatory reform).

18. S. 2195, 104th Cong. (1996).

19. See *id.*

20. See CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, PROPOSED APPROACH TO REGULATION OF CELLULAR AND TISSUE-BASED PRODUCTS (FDA Docket No. 97N-0068), Feb. 28, 1997 [hereinafter CELLULAR & TISSUE-BASED PRODUCTS].

tifically sound proposal to treat cord blood as an investigatory new drug subject to a period of clinical development.

II. CORD BLOOD TRANSPLANTATION: A PRIMER

A. *A Brief History of Stem Cell Transplantation*

The harvesting of bone marrow stem cells for allogenic (one person to another) transplantation began in the 1960s and soon became an important medical intervention.²¹ The typical bone marrow transplant recipient is a leukemia victim, but bone marrow transplantation (BMT) is also used to treat other disorders, particularly anemias and immune system dysfunction. Most recently, BMT has been used in the experimental treatment of organ and inoperative metastatic cancers.²²

As an alternative to BMT, researchers can now harvest hematopoietic stem cells from a patient's own peripheral (circulatory) blood. This stem cell collection technique is most often used prior to cancer therapy, when stem cells are harvested from a patient's blood and then reintroduced after treatment, in anticipation that the patient's bone marrow will be unavoidably damaged by high-dose chemotherapy and radiation.²³ Peripheral stem cells are harvested in a process called *apheresis*, in which blood is circulated through a machine that removes the cells from the patient's bloodstream. Apheresis requires two to four hours per session, and the extraction process must be repeated an average of six times to obtain a sufficient concentration of stem cells for transplantation.²⁴

21. See NATIONAL CANCER INSTITUTE, RESEARCH REPORT: BONE MARROW TRANSPLANTATION AND PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (NIH Publication No. 95-1178), Nov. 1994 [hereinafter NCI REPORT]. The NCI REPORT is available online at <<http://cancernet.nci.nih.gov>>. The page numbers cited in this article will refer to the online version of the NCI REPORT.

22. See *id.* at 3.

23. See *id.* Chemotherapy and radiation target cells that are dividing; thus, these treatments destroy both cancer cells and bone marrow stem cells. Destruction of the bone marrow cells may be a deliberate component of treatment for leukemia and related blood disorders, or simply an inadvertent consequence of radiation and chemotherapy for other disorders. See *id.*

24. See *id.* at 7.

Both BMT and peripheral blood stem cell transplantation involve significant cost and donor inconvenience. Both techniques also require a high degree of histocompatibility between donor and recipient.²⁵ To maximize the possibility of a successful transplant, surgeons usually require a match between donor and recipient on five of six human leukocyte-associated antigens (HLAs), which are proteins found on the surface of cells.²⁶

The ideal stem cell donor is a sibling who shares the same HLA genotype as the patient, but such matches occur less than 30% of the time. With a current demographic trend toward smaller family sizes, the likelihood of finding HLA-identical siblings will continue to decrease.²⁷ Unrelated donors who match with the patient on a sufficient number of HLA antigens are also quite difficult to find, especially when patients belong to racial and ethnic minorities whose numbers are underrepresented in computerized donor registries.²⁸ Due to the difficulty of finding a matched source of donor stem cells, thousands of leukemia victims and other patients die each year prior to obtaining a transplant.²⁹

In a stem cell transplant, a patient's damaged blood production system is purposely (or inadvertently, as a result of treatment for some cancers) destroyed by chemotherapy and radiation. The donor's hematopoietic stem cells are then introduced

25. See Dr. Richard Champlin, M.D., Chairman of the Department of Hematology, Anderson Cancer Center, Remarks at the Peripheral Blood Stem Cell Workshop 24 (FDA Center for Biologics Evaluation and Research, Feb. 22, 1996) [hereinafter *Peripheral Blood Workshop*]. The transcript of the workshop is available at the Documents Management Branch of the FDA. See *supra* note 16.

26. See NCI REPORT, *supra* note 21, at 4.

27. See Dr. John Hansen, Fred Hutchinson Cancer Research Center, Remarks at the Workshop on Cord Blood Stem Cells: Discussion of Procedures for Transplantation and Storage 75 (FDA Center for Biologics Evaluation and Research, Dec. 13, 1995) [hereinafter *Cord Blood Workshop*]. The transcript of the workshop is available at the Documents Management Branch of the FDA. See *supra* note 16.

28. See Silberstein & Jefferies, *supra* note 4, at 206.

29. See NCI REPORT, *supra* note 21, at 4. It is important to note, however, that BMT does not invariably result in a cure. Many transplant patients die every year *in spite of* BMT, due to transplant failure or relapse, or, in some cases, *because of* BMT, if they experience graft versus host disease or other transplant-related complications. For a discussion of transplant-related complications, see generally *Cord Blood Workshop*, *supra* note 27.

into the patient's blood stream in an attempt to repopulate the patient's blood supply with new cells.³⁰

Successful repopulation or *engraftment*, in which the transplanted stem cells migrate to the patient's bone marrow and begin to produce new blood cells, often fails to occur.³¹ Even when engraftment is achieved, in many cases the patient's body is then assailed by the donor's foreign cells in a reaction known as *graft-versus-host disease* (GVHD).³² This disease is related to the degree of histocompatibility between donor and recipient and occurs when infection-fighting cells in the donated marrow attack the transplant recipient's body.³³ GVHD can occur immediately or years after the transplant procedure, and severe cases of GVHD are often fatal. Some researchers think that paradoxically, mild cases may actually protect the transplant patient against relapse, if the activated donor cells also kill residual cancer cells in the recipient's body (termed the *graft-versus-cancer effect*).³⁴

The past decade witnessed the introduction of a new and exciting alternative to conventional sources of hematopoietic stem cells: blood drawn at birth from the umbilical cord or the placenta. This so-called "cord" blood is simple to obtain, and it turns out to be rich in hematopoietic stem cells. The potential value of placental and umbilical cord blood, which has long been considered medical waste,³⁵ was first recognized in 1988 by two scientists, cancer researcher Edward Boyse and hematologist Hal Broxmeyer.³⁶ Together, Boyse and Broxmeyer engineered the first transplant of cord blood stem cells between a young patient with the rare blood disease Fanconi's anemia and an unaffected sibling.³⁷ Since that groundbreaking 1988 procedure, over 200 allogenic cord blood stem cell transplants have been performed, and the initial rates of survival and GVHD incidence compare favorably to statistics for BMT.³⁸

30. See NCI Report, *supra* note 21, at 5.

31. See *id.* at 8.

32. See *id.* at 10.

33. See *id.*

34. See *id.* at 10-11.

35. See Roni Rabin, *Bloodline*, *NEWSDAY*, Apr. 9, 1996, at B19.

36. See Cohen, *supra* note 3, at 13.

37. See *id.* at 13-14.

38. See Jean-Philippe Laporte et al., *Cord Blood Transplantation from an Unre-*

The ultimate promise of cord blood stem cell transplantation may some day be realized through gene therapy. If researchers eventually succeed in causing cord blood stem cells to take up new genes, the rapidly-dividing stem cells could then produce legions of genetically-altered progeny within the transplant recipient's body.³⁹ Researchers hope that these manipulated stem cells could be used to replace or alter the function of genes known to be defective in a growing list of diseases. Clinical breakthroughs in gene therapy have been slow to arrive, however, the use of stem cells to cure genetically-transmitted diseases remains only a theoretical possibility.⁴⁰

Nonetheless, the immediate clinical utility of cord blood was such that in 1992, the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (NIH) decided to fund a pilot cord blood bank at the New York Blood Center.⁴¹ This study provided the initial evidence that cord blood could feasibly be harvested, stored and transplanted between unrelated child donors and recipients. In an expanded thirty million dollar project,⁴² NHLBI will now establish a network of public cord blood banks under a research protocol addressing optimal methods of cord blood collection and storage.⁴³ Researchers in the NHLBI study will also examine whether cord blood transplantation might be a successful treatment for adult

lated Donor in an Adult with Chronic Myelogenous Leukemia, 335 NEW ENG. J. MED. 167, 167 (1996).

39. See Joan Stephenson, *Terms of Engraftment: Umbilical Cord Blood Transplants Arouse Enthusiasm*, 274 JAMA 1813, 1814 (1995).

40. See NATIONAL RESEARCH COUNCIL INSTITUTE OF MEDICINE, ASSESSING GENETIC RISKS, IMPLICATIONS FOR HEALTH AND SOCIAL POLICY 150 (1995) [hereinafter ASSESSING GENETIC RISKS]. One cord blood transfusion involving gene therapy was attempted in 1995. In that case, stem cells carrying the gene for the enzyme adenosine deaminase (ADA) were transplanted into three children with ADA deficiency. Longitudinal data are needed to determine the success or failure of this experiment. See generally D.B. Kohn, *Gene Therapy for Hematopoietic and Immune Disorders*, 18 BONE MARROW TRANSPLANTATION 55, 55-58 (1996); T. Moritz et al., *Human Cord Blood Cells as Targets for Gene Transfer: Potential Use in Genetic Therapies of Severe Combined Immunodeficiency Disease*, 178 J. EXP. MED. 529 (1993).

41. See Letter from Claude Lenfant, Director, NHLBI, to the FDA 1 (July 25, 1996) (on file with the FDA).

42. See Cohen, *supra* note 3, at 13.

43. See *id.*; see also Letter from Lenfant, *supra* note 41, at 1-2.

patients, or for patients whose HLA antigen-type does not closely match that of the cord blood donor.⁴⁴

B. *The Cord Blood Controversy*

Cord blood banking became controversial as a result of a growing phenomenon in American science: the entry of venture capital at an early phase in the development of a scientific field, through profit-oriented collaborations between academic scientists and biotechnology entrepreneurs.⁴⁵ Changes in federal law have created economic incentive for such collaboration, thus speeding the commercial application of new research discoveries.⁴⁶

The commercialization of cord blood happened relatively quickly. Following the success of the first cord blood transplant, Broxmeyer, Boyse, and several other researchers patented their technique, sought venture capital, and founded Biocyte Corp., the original for-profit cord blood bank.⁴⁷ Since the field of cord blood banking was unregulated, barriers to entry were low, and other private ventures soon followed. When concerns about the marketing and storage practices of the for-profits (and, in some cases, of the nonprofit cord blood storage centers⁴⁸) came to the attention of the FDA, the agency formed a task force with representatives from all interested parties, and eventually put forth the first of two draft proposals for a regulatory strategy.

C. *FDA's Draft Proposals for Cord Blood Regulation*

The central and most controversial aspect of the FDA's initial draft approach was a proposal to treat cord blood cells similarly

44. See Letter from Lenfant, *supra* note 41, at 1-2.

45. See Cohen, *supra* note 3, at 15.

46. See generally Thomas N. Bulleit, Jr. & Suzanne M. Bonnet, *Technology Transfer: Trends in the Federalization of Biomedical Research*, 71 ACAD. MED. 709 (1996).

47. See Cohen, *supra* note 3, at 14-15.

48. One concern with the New York Blood Center trial was the practice of not retaining donor identity for potential follow-up. By current consensus, it is now generally agreed that donor identities must be retained with cord blood specimens. See Jeffery McCullough et al., *Proposed Policies and Procedures for the Establishment of a Cord Blood Bank*, 20 BLOOD CELLS 609, 614 (1994).

to experimental new drugs, by imposing the rules that govern the Investigational New Drug (IND) process.⁴⁹ IND regulations prohibit the marketing and commercialization of a new drug until sufficient data exists to develop licensing, labeling, and manufacturing standards.⁵⁰ In February, 1996, the FDA suggested that only when the IND period of clinical development was complete would cord blood banks be permitted to apply for various licenses that permit the commercial production of biologics.⁵¹ Until such time, all cord blood banking and transplantation would be conducted on a nonprofit basis, under FDA-approved research protocols.⁵²

In a February 1997 modification of this initial proposal, the FDA suggested that the agency would exempt the storage and transplantation of autologous cord blood samples, and samples intended for use in a first degree blood relative, from IND regulations and associated premarket approval restrictions.⁵³ Entities, public or private, that did not store cord blood for the purpose of allogenic transplant would only be required to comply with FDA-established standards and procedures for the handling and storage of cord blood specimens.⁵⁴ This latter proposal, while partially preserving a period of clinical development, would also allow significant commercialization of cord blood storage in the face of many unanswered questions about the safety, efficacy, and ethics of cord blood transplantation.⁵⁵

Arguably, the FDA has the discretion to dispense with premarket approval requirements altogether. Should the agency conclude that the commercial and the clinical (non-research) use of cord blood is appropriate at this time, the FDA could simply designate cord blood as a well-characterized biologic, and deem the transplantation of cord blood specimens to fall within the traditionally unregulated "practice of medicine." The agency could then adopt and enforce the processes and standards pro-

49. See CORD BLOOD DRAFT DOCUMENT, *supra* note 15.

50. See John A. Norris, *Fulfilling FDA's Vision of Faster Drug Review*, FDA CONSUMER, Jan. 1988, at 7, 7.

51. See CORD BLOOD DRAFT DOCUMENT, *supra* note 15.

52. See *id.*

53. See CELLULAR & TISSUE-BASED PRODUCTS, *supra* note 20.

54. See *id.*

55. See discussion *infra* Parts II.E, III.

posed by the cord blood industry,⁵⁶ without subjecting cord blood to exacting requirements of efficacy and potency.⁵⁷ Opponents of IND regulations for cord blood regard the FDA as the source of costly and unnecessary delays caused by the imposition of a complicated regulatory framework for new medical products.⁵⁸

D. *Current Food and Drug Regulatory Schemes*

Statutory authorities extend the regulatory reach of the FDA broadly to encompass the oversight of one trillion dollars worth of drugs and consumer products per year.⁵⁹ In a 1996 speech, FDA Commissioner Kessler described his agency as "the most important consumer protection agency in the world," while at the same time he acknowledged tension between the agency's regulatory function and an equally critical mission, that of "getting new therapies to people who need them."⁶⁰ To this latter end, the FDA has always maintained that it "treads lightly" upon the practice of medicine and surgery.⁶¹ Agency officials have expressed the desire to collaborate with industry, academia, and the medical community in a cooperative approach to establishing regulatory oversight for new products.⁶² Currently, the FDA is confronting significant deregulatory pressures from Congress and from powerful industry groups,⁶³ such that the final outcome of new regulatory proposals may ultimately be shaped as much by political forces as by scientific considerations.⁶⁴

56. See, e.g., Letter from Thomas Moore, President, Cord Blood Registry, to the FDA (July 26, 1996) (suggesting that the Foundation for the Accreditation of Hematopoietic Cell Therapy should work with industry and medical groups to establish quality assurance and registration standards for cord blood transplantation).

57. See Edward L. Korwek, *Human Biological Drug Regulation: Past, Present, and Beyond the Year 2000*, FOOD & DRUG L.J., 50th Anniversary Issue, Spring 1995, at 123, 129.

58. See generally Public Comments submitted to the FDA, *supra* note 16.

59. See *The Food and Drug Administration: An Overview* (visited March 30, 1998) <<http://www.fda.gov>>.

60. David Kessler, FDA Commissioner, Address to the Food and Drug Law Institute, Washington, D.C. (Dec. 19, 1996).

61. See *id.*

62. See Philip D. Noguchi, *From Jim to Gene and Beyond: An Odyssey of Biologics Regulation*, 51 FOOD & DRUG L.J. 367, 373 (1996).

63. See Walsh & Pyrich, *supra* note 17, at 887.

64. See discussion *infra* Parts IV, V (discussing policy considerations of cord blood

The FDA's regulation of new drugs and medical therapies is complex, and at times, unwieldy.⁶⁵ The regulation of biological products in particular has been forced to evolve in response to rapid advances in pharmaceutical research and biotechnology. The following discussion will summarize the FDA's current regulatory framework for drugs and other medical products and will highlight some of the definitional and jurisdictional issues that the FDA has faced in overseeing the use of human blood and blood components.

For the purposes of regulation, the FDA divides the universe of medical products into three categories: (1) drugs; (2) medical devices; and (3) biologics.⁶⁶ The definitional boundaries of these categories are expansive and overlapping. For example, under the Federal Food, Drug, and Cosmetics Act (FFDCA) and related amendments,⁶⁷ a drug is defined as any product "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals."⁶⁸ Reviewing courts have granted the FDA great discretion to fashion its own interpretation of the statutory language governing the classification of products, under the rationale that broad agency discretion is consistent with FDA's responsibility to protect the public health.⁶⁹

regulation and specifically the Tissue Act and its consequences).

65. See John C. Petricciani, *Reinventing the Biologics Approval Process*, 51 FOOD & DRUG L.J. 139, 140 (1996) (stating that current system of product jurisdiction "is neither logical nor efficient").

66. See Section 201(g)(1) of the Federal Food, Drug & Cosmetic Act, 21 U.S.C. 321(g)(1) (1994) (defining "drugs"); Section 201(h) of the Federal Food Drug & Cosmetic Act, 21 U.S.C. 321(h) (1994) (defining "device"); Section 351(a) of the Public Health Service Act, 42 U.S.C. 262(a) (1994) (defining "biological product"). It should be noted that some complex products are combined drugs, devices, and/or biologics. For example, cigarettes are considered a device for the delivery of the drug nicotine. Similarly, gene therapy utilizes biological products that are both therapeutic drugs and the delivery devices. See generally Cohen, *supra* note 3.

Under the FDA's interpretation of the Safe Medical Devices Act of 1990, 21 U.S.C. §§ 321, 333, 351, 353, 360(c)-(j), 360(l), 360(hh)-(ss), 383; 42 U.S.C. § 263(b)-(n) (1994), the agency has discretion to determine the primary mode of action for a product and to select the most appropriate regulatory classification. See Prohibition of Sale and Distribution to Persons Younger Than 18 Years of Age, 21 C.F.R. §§ 897.10, 897.12, 897.14, 897.16 (1997) [hereinafter FDA Tobacco Regulations].

67. 21 U.S.C. §§ 301-95 (1994).

68. *Id.* § 321(g)(1).

69. See, e.g., *United States v. An Article of Drug . . . Bacto-Unidisk*, 394 U.S. 784, 800 (1969) (noting that the FDA may interpret the meaning of the term "drug"

1. Drugs

New drugs must receive FDA approval prior to marketing. Through the premarket approval process, the FDA requires that, before advertising a drug or selling it for a profit, a sponsor must demonstrate that the drug is both safe and effective for its intended uses.⁷⁰

The approval process begins when a drug's sponsor, after having collected sufficient data about the effects (therapeutic and toxic) of the drug in laboratory animals, applies to the FDA for an investigatory new drug exemption (IND).⁷¹ Since the FDCA prohibits the distribution of drugs that have not yet been approved by the FDA, the agency must grant investigators an exemption from the statute to permit the use of an unapproved drug in research with human subjects.⁷²

If the FDA grants the IND exemption, the sponsor may begin the first of three phases of clinical (human) trials.⁷³ Phase I trials are small-scale studies conducted with healthy volunteers, largely for the purpose of determining a drug's short-term side effects and toxicity.⁷⁴ If levels of risk appear acceptable, Phase II testing will be authorized in a larger sample of patients, usually several hundred individuals. Phase II testing normally involves randomized controlled trials to investigate whether the drug is effective for its intended use.⁷⁵ The timeline to completion of Phase II testing is normally two to three years from approval of the IND.⁷⁶

If data from Phases I and II suggest that the drug is both safe and effective, the FDA will authorize Phase III testing, in which researchers administer the new drug to an even broader

broadly, consistent with the agency's mission to protect public health); *see also* FDA Tobacco Regulations, *supra* note 66.

70. *See, e.g.*, FDA Tobacco Regulations, *supra* note 66, at § 897.30.

71. *See id.*

72. *See* Walsh & Pyrich, *supra* note 17, at 903 (discussing "The Drug Approval Process").

73. *See* 21 U.S.C. § 355(i) (1994); 21 C.F.R. § 312.20-23 (1997).

74. *See* Ken Fleiger, *Testing In 'Real People,'* FDA CONSUMER, Jan. 1988, at 13, 13-14.

75. *See id.*

76. *See id.*

range of patients in an attempt to simulate the conditions of actual clinical use and thereby confirm effectiveness, determine appropriate dosages, labeling requirements, and longer-term side effects.⁷⁷ Phase III trials typically last one to four years. Of all the new drugs for which INDs are submitted, only 25-30% will clear Phase III testing.⁷⁸

After completion of all clinical trials, the drug sponsor files a New Drug Application (NDA) with the FDA.⁷⁹ The NDA is a comprehensive document containing virtually all available data about the drug and its known effects. An NDA may consist of over 100,000 pages of study results,⁸⁰ and the FDA's review of an NDA often takes several years, although the agency now has expedited procedures for high-priority drugs.⁸¹

Once a drug is approved for marketing, manufacturers must comply with extensive regulations regarding drug labeling and advertisement.⁸² Manufacturers must also submit periodic reports of adverse events (i.e., side effects, complications, or deaths) associated with the use of the drug. At its discretion, the FDA may also require postmarket surveillance studies, known as Phase IV testing, that will enable the systematic study of adverse events.⁸³ In addition to monitoring adverse events, the FDA will establish standards for the manufacturing, processing, storage, and shipment of drugs. These standards, known as Good Manufacturing Practices (GMPs), allow the FDA to inspect facilities and sanction manufacturers for the failure to comply with these GMPs.⁸⁴

77. See *id.*

78. See *id.*

79. See Walsh & Pyrich, *supra* note 17, at 908.

80. See Norris, *supra* note 50, at 7.

81. See Dixie Farley, *Benefit v. Risk: How FDA Approves New Drugs*, FDA CONSUMER, Jan. 1995, at 23, 24-25.

82. See generally 21 U.S.C. § 351 (1994) (addressing false advertisement and labeling); *id.* § 352 (providing that false and misleading drug advertising is specifically prohibited); see also Walsh & Pyrich, *supra* note 17, at 912.

83. See Walsh & Pyrich, *supra* note 17, at 914.

84. See 21 U.S.C. § 351(a)(2) (1994).

2. Devices

Until the mid 1970s, medical devices were subject only to limited postmarket safety and labeling requirements.⁸⁵ The FDA did not obtain full regulatory authority (including premarket approval authority) over medical devices until the passage of the Medical Device Amendments to sections 301-360 of the FFDCA,⁸⁶ and the subsequent Safe Medical Devices Act of 1990.⁸⁷

Under these statutes, a medical device is considered to be a therapeutic product that “does not achieve its primary intended purpose through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.”⁸⁸ The FDA’s regulatory scheme classifies medical devices in a three-tiered system of escalating product controls, based upon the risk that a particular device poses to consumers. As with drugs, new devices are subject to premarket approval, advertising, labeling, and manufacturing regulations, and certain postmarket reporting and surveillance requirements.⁸⁹

3. Biologics

This category comprises products derived from living materials—humans, plants, animals, or microorganisms—when such products are used in the treatment or prevention of disease.⁹⁰ The Public Health Service Act (PHSA)⁹¹ defines biological

85. See Walsh and Pyrich, *supra* note 17, at 903.

86. Pub. L. No. 94-295, 90 Stat. 539 (codified as amended 15 U.S.C. § 55; 21 U.S.C. §§ 321(y), 331(e), 331(j), 331(l), 331(p)-(r), 334(a), 351(e)-(i), 352(e), 352(j), 352(o), 360(a)-(e), 360(i)-(k), 374(a), 374(e), 374(g), 374(r), 379(a); 42 U.S.C. § 3512 (1994)).

87. Pub. L. No. 101-629, 104 Stat. 4511 (codified at 21 U.S.C. §§ 321, 333, 351, 353, 360(c)-(j), 360(l), 360(hh)-(ss), 383; 42 U.S.C. § 263(b)-(n) (1994)).

88. 21 U.S.C. § 321(h) (1994).

89. See Walsh & Pyrich, *supra* note 17, at 918-29 (discussing in detail medical device regulation).

90. See Statement by Michael Beatrice of FDA’s Center for Biologics Evaluation and Research (CBER), in Kevin L. Ropp, *Just What is a Biologic, Anyway?*, FDA CONSUMER, Apr. 1993, at 27, 27.

91. See scattered provisions of Title 42 of the United States Code.

products as "any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or its derivatives (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of diseases or injuries of man."⁹² Biologics were originally regulated under a statutory scheme distinct from the one applied to foods and drugs, and regulatory authority over biologics was vested in the National Institutes of Health until jurisdiction was subsequently transferred to the FDA in 1972.⁹³

Because living materials are used in their manufacture, biological products are more fragile than drugs or medical devices, and the composition of biologics is more difficult to standardize.⁹⁴ Unlike the chemical compounds that make up a drug or the inert parts of a medical device, most components of a biologic are highly sensitive to heat, light, contamination, motion, and temperature.⁹⁵ Additionally, while drug composition and purity can be determined by chemical analysis, not every component of a biological product can be easily identified or measured.⁹⁶ For these reasons, oversight of manufacturing and processing is a particularly important aspect of biologics regulation, and both biological products and the facilities that manufacture them must meet licensing requirements.⁹⁷

The emergence of new hybrid therapeutics or "biological drugs"⁹⁸ such as cord blood highlighted a significant gap in the PHS statute: the scheme had no provisions requiring a manufacturer to prove that a new biologic is chemically effective. Under the broad statutory reach of the FFDCA, however, the FDA has determined that biologics also fall simultaneously under the regulatory provisions applicable to either drugs or medical devices.⁹⁹ The FDA has the discretion, therefore, to extend the requirement of an IND exemption to new biological

92. 42 U.S.C. § 262(a) (1994).

93. See 37 Fed. Reg. 12,865 (1972); see generally Korwek, *supra* note 57.

94. See Ropp, *supra* note 90, at 27-28.

95. See *id.* at 28.

96. See *id.*

97. See *id.*

98. *Id.*

99. See 21 C.F.R. § 312.2 (1997).

drugs and to require a showing of clinical effectiveness prior to marketing.¹⁰⁰ Duplicate premarket approvals of the new product are not required. If the FDA asks a manufacturer to submit both the product and the establishment license applications that the PHS Act requires for a biologic, then the agency will not also require a manufacturer to submit an NDA for the same product.¹⁰¹

In 1998, the regulatory scheme for biological products will undergo several important changes. As the various provisions of the Food and Drug Administration Modernization and Accountability Act (and implementing regulations)¹⁰² take effect, the FDA's regulation of biologics will be streamlined and harmonized with the agency's drug regulations. The new law calls for a single biologics license (BLA) that is intended to cover both the biological product and the manufacturing facility.¹⁰³ As implementing regulations are promulgated, standards for biologics approval will be altered to resemble more closely the current standards for drug approval.

E. *Blood as a Biological "Drug"*

Effective regulation of biologics has proven difficult because the field of biological therapeutics is changing so rapidly.¹⁰⁴ Under the FDA's conceptual framework, the categories of "drug" and "biologic" are not mutually exclusive; rather, the agency envisions that new biological products used to treat, prevent, or cure diseases should be held to safety and effectiveness standards at least as stringent as those for conventional drugs.¹⁰⁵ In furtherance of this goal, the FDA's regulatory policies are evolving in tandem with the development of new biotechnologies, but this evolution sometimes produces dissimilar requirements for what seem to be similar products.

100. *See id.*

101. *See* CORD BLOOD DRAFT DOCUMENT, *supra* note 15.

102. Pub. L. No. 105-115, 111 Stat. 2323 (1997).

103. *See id.*

104. *See* Noguchi, *supra* note 62, at 368 ("[C]ell and gene therapies continue to challenge existing statutes and regulations.").

105. *See* Ropp, *supra* note 90, at 28.

Blood and blood components are one example. Today, cord blood stem cells intended for transplantation would be considered a "therapeutic" serum, thereby meeting the definition of a biological drug and triggering the safety and effectiveness requirements of premarket approval.¹⁰⁶ Yet historically, the FDA has not required blood banks to submit INDs or to provide premarket safety and effectiveness data for blood intended for transfusion. Nor does the FDA subject hematopoietic stem cells derived from bone marrow or from adult peripheral (circulatory) blood to premarket approval, unless such cells are "substantially manipulated" or genetically altered to create new somatic cell therapies.¹⁰⁷ Under the FDA's first proposal for cord blood regulation, however, hematopoietic stem cells derived from cord blood would be subjected to the IND mechanism irrespective of the extent to which the cells are manipulated prior to transplantation.¹⁰⁸

On the whole, this regulatory disparity reflects changed expectations about the standards of safety and effectiveness that new biologics must meet. Bone marrow transplantation was developed prior to the era of strict FDA oversight of biological therapies and, under the congressionally authorized National Bone Marrow Donor Program of 1986,¹⁰⁹ voluntary industry standards are the primary form of regulation for the collection and use of hematopoietic stem cells derived from bone marrow. When Congress established the Bone Marrow Donor Program as a statutory mechanism for oversight of BMT, the FDA abstained from further regulation, deeming bone marrow transplantation activities to fall under the purposely-unregulated practice of medicine.¹¹⁰ On the heels of the HIV epidemic and a nationwide scare about the safety of blood banks, however,

106. See 21 C.F.R. 600 (1997); see also Ropp, *supra* note 90, at 28.

107. See CENTER FOR BIOLOGICS EVALUATION AND RESEARCH, FOOD AND DRUG ADMINISTRATION, DRAFT DOCUMENT CONCERNING THE REGULATION OF PERIPHERAL BLOOD HEMATOPOIETIC STEM CELL PRODUCTS INTENDED FOR TRANSPLANTATION OR FURTHER MANUFACTURE INTO INJECTABLE PRODUCTS, Feb. 1996 [hereinafter PERIPHERAL BLOOD DRAFT DOCUMENT]; see also, APPLICATION OF CURRENT STATUTORY AUTHORITIES TO HUMAN SOMATIC CELL THERAPY PRODUCTS AND GENE THERAPY PRODUCTS, 58 Fed. Reg. 53,248 (1993).

108. See PERIPHERAL BLOOD DRAFT DOCUMENT, *supra* note 107.

109. See Cohen, *supra* note 3, at 27.

110. See *id.*

the FDA has begun to take a far more cautious approach toward biologics regulation.¹¹¹

The cord blood industry and some researchers favor the BMT model of private-sector oversight for new biologics; these opponents of new regulation would also prefer that the FDA adopt a uniform approach to all blood products.¹¹² For the purpose of federal regulation, researchers such as Dr. Harvey Klein of the NIH insist that "blood is blood."¹¹³ Klein and others argue that, to the extent that the transplantation of cord blood is a novel use of a blood component, such a use should fall within the unregulated practice of medicine.¹¹⁴ In lieu of an entirely new set of manufacturing regulations, these researchers believe that cord blood can be safely collected and processed using standard blood-banking procedures.¹¹⁵

Proponents of industry self-regulation argue that requiring the IND process for cord blood stem cells, but not for stem cells derived from bone marrow or from adult peripheral blood, equates to illogically disparate treatment of similar products.¹¹⁶ Oversight of the harvesting and use of cord blood stem cells, the proponents maintain, can best be accomplished through voluntary adherence to industry-developed standards.¹¹⁷ The merits of this claim may be evaluated by examining the scientific debate over the maturity of the cord blood transplantation field, and the legal and policy issues arising from the commercialization of cord blood.

111. See Jeffery Goldbert, *Next Target: Nicotine*, THE N.Y. TIMES MAG., Aug. 4, 1996, at 24 (noting that the FDA now closely regulates the nation's blood supply after the agency found "widespread weaknesses" in the Red Cross system of tracking donors and screening donated blood).

112. See Letter from Alan Goldhamer, Director of Technical Affairs, Biotechnology Industry Association, to the FDA 1 (Apr. 25, 1996) (on file with the FDA).

113. See Letter From Harvey G. Klein, Chief of Transfusion Medicine, NIH Clinical Center, to the FDA, 1 (Mar. 26, 1996) (on file with the FDA).

114. See discussion *supra* Part II.D (discussing the FDA regulatory scheme).

115. See, e.g., Letter from Moore, *supra* note 56, at 1 (stating that the processing of cord blood samples prior to storage involves only "minor, well-established, and safe laboratory procedures").

116. See *id.*

117. See *id.*

III. SCIENTIFIC AND SAFETY CONCERNS IN PLACENTAL/ UMBILICAL CORD BLOOD TRANSPLANTATION

A. *Are Cord Blood Stem Cells "Investigational" Drugs or "Well Characterized" Blood Products?*

Scientifically, the extent of the similarity between cord blood stem cells and stem cells derived from bone marrow or peripheral blood is debatable. Some researchers describe cord blood stem cells as qualitatively and quantitatively distinct from the stem cells found in samples of bone marrow and peripheral blood.¹¹⁸ Other researchers insist that all hematopoietic stem cells are basically the same.¹¹⁹ Whether stem cells from different sources are indeed similar remains an unanswered question because no one has ever identified a human stem cell under a microscope. To date, the presence of hematopoietic stem cells in specimen blood can only be inferred from the presence of biological markers such as more mature daughter cells.¹²⁰

The question of similarity is an important one. If cord blood stem cells are not well-characterized blood products, by definition cord blood storage and transplantation have unknown efficacy and pose novel safety risks that must be better understood prior to commercial use. On the other hand, if cord blood cells used for transplantation are functionally indistinguishable from

118. See Letter from Craig W.S. Howe, CEO, National Marrow Donor Program, to the FDA 1 (July 26, 1996) (on file with the FDA) ("It is quite clear, however, that these stem cells differ from marrow cells both quantitatively and qualitatively. Additionally, the immunocompetent lymphocytes in cord blood are dramatically dissimilar from those in marrow blood.").

119. For example, Dr. Robertson Parkman, Director of the Bone Marrow Transplant Program at Children's Hospital in Los Angeles, has stated that "biologically we view all hematopoietic stem cells as the same, that based on clinical settings, the decisions about how you choose to get them will vary. And that is the most logical way to look at them, rather than this fragmentation that is being set forth." Dr. Robertson Parkman, Remarks at the Biological Response Modifiers Advisory Committee 268 (Feb. 28, 1996). The transcript of the committee hearing is available at the Documents Management Branch of the FDA. See *supra* note 16.

120. See Dr. Yong-Hoon Lee, Branch Chief for the Blood and Plasma Branch of the Division of Blood Applications, Office of Blood, CBER, FDA, Remarks at the Peripheral Blood Workshop, *supra* note 25, at 13 ("One of the problems is that we really don't know how to clearly identify what a stem cell is. We know what a stem cell does. We know what the phenotype of a subset containing stem cells is, but one cannot identify individual stem cells *per se*").

other hematopoietic stem cells, and if cord blood stem cells pose no novel risks, then the FDA's lengthy and costly process of new drug investigation may be unwarranted.

Although researchers have not resolved the question of the actual physiological similarity between stem cells derived from cord blood and those from bone marrow or peripheral blood, there is evidence for a functional dissimilarity between cord blood stem cell *transplants* and transplants of stem cells from other sources. For example, the same properties of cord blood that appear to convey less risk of graft versus host disease¹²¹ may ultimately leave the recipient of a cord blood transplant more prone to relapse.¹²² Another possible disadvantage of cord blood transplants, pending the development of techniques to artificially expand the quantity of stem cells in a specimen) is that only one unit is available per transplant procedure, and the amount in an individual specimen may be insufficient to achieve engraftment.¹²³

Because both mother and infant must be tested for infectious diseases such as hepatitis and HIV, cord blood donations are more difficult to screen than bone marrow from adult donors.¹²⁴ Genetic screening of cord blood donations is particularly problematic. Although an adult bone marrow donor has an established medical history, the newborn cord blood donor is a

121. Cord blood lymphocytes appear relatively immature, potentially allowing for a greater degree of HLA antigen disparity between donor and recipient, and possibly reducing the risk and severity of graft versus host disease. See generally H.E. Broxmeyer et al., *Human Umbilical Cord Blood as a Potential Source of Transplantable Hematopoietic Stem/Progenitor Cells*, 86 PROC. NAT'L ACAD. SCI. U.S.A. 3828 (1989); M.Y. Gordon et al., *Probability of Progenitor Renewal (PPR) and Production of Clonogenic Progeny (CFU-GM) by Primitive Adherent Progenitor Cells in Adult Human Bone Marrow and Umbilical Cord Blood*, 90 BR. J. HAEMATOLOGY 744 (1995); J.E. Wagner et al., *Allogeneic Sibling Umbilical Cord Blood Transplantation in Children with Malignant and Non-malignant Disease*, 346 LANCET 214 (1995).

122. According to transplant specialist Joanne Kurtzberg of Duke Medical Center, "[an] unresolved problem is whether the lower incidence of GVHD indicates a decrease in graft-versus-leukemia activity and thus an increase in the risk of leukemic relapse." Joanne Kurtzberg et al., *Placental Blood as a Source of Hematopoietic Stem Cells for Transplantation into Unrelated Recipients*, 335 NEW ENG. J. MED 157, 165 (1996).

123. It should be noted that banked placental/umbilical blood may be procured for transplant quickly, in contrast to the four to six months often required to find an unrelated bone marrow donor. See *id.*

124. See McCullough et al., *supra* note 48, at 609.

medical "blank slate."¹²⁵ This lack of a medical history militates toward the most extensive screening possible prior to the use of a cord blood sample in transplantation.

But genetic tests do not yet exist for most diseases, and if they did, testing for the full range of known genetic diseases might be prohibitively expensive and impractical. Furthermore, even if both parents and infant were to receive every genetic test currently conceivable, the pairing of maternal and paternal genes could produce new mutations that would be carried undetected in the infant's DNA.¹²⁶

Long-term cryostatic storage of a newborn donor's own cord blood—in anticipation that the blood might be used to treat some hypothetical illness in the donor herself—is also unique to the cord blood field. Such a use of stem cells can hardly be characterized as anything other than experimental, because to date, banked autologous blood has never been used for a transplant. Cord blood transplants are currently performed with allogenic stem cells that have been frozen for relatively short periods of time.¹²⁷

At present, there is little evidence that cord blood samples in long term storage remain safe and effective for use, because blood products are typically stored for less than thirty days.¹²⁸ Nor is there any evidence that autologous transplants are preferable to cord blood from a matched but unrelated donor. An autologous transplant could reintroduce genetically-transmitted disease; such a transplant would also test the possibility that a donor's own stem cells might not perceive the body as a foreign host, causing stem cell progeny to fail to mount the proper immune response when they encounter diseased cells.¹²⁹ In fact, Joanne Kurtzberg, who has performed more cord blood transplants than any other researcher in the field, stated in her written comments to the FDA that transplanting physicians

125. See Letter from Howe, *supra* note 118, at 1.

126. See *id*; see also McCullough et. al, *supra* note 48, at 609.

127. See Silberstein & Jefferies, *supra* note 4, at 200; see also Robin DeRosa, *Blood Treatment Promises Much But Needs Regulation*, USA TODAY, July 12, 1996, at 12A.

128. See Cohen, *supra* note 3, at 27.

129. See Statement of Dr. Paul McCurdy of NHLBI, in Cohen, *supra* note 3, at 31-32.

might well refuse to use autologous cord blood because of such unresolved safety and efficacy issues.¹³⁰

Other essential scientific questions regarding the safety and efficacy of cord blood remain unanswered. For example, researchers have not yet determined through controlled trials which methods of processing, freezing, and thawing samples are adequate for long-term storage and reuse.¹³¹ Nor is it known what minimal amount of cord blood is necessary for engraftment, particularly in adults.¹³² Cord blood has been touted as requiring a less precise matching of HLA antigens between donor and recipient, but the extent to which transplants can be mismatched without posing a threat to recipients is unknown.¹³³

Additionally, while cord blood storage has been promoted as a universal form of health "insurance" that every parent should consider,¹³⁴ a range of factors contraindicate the harvesting and subsequent use of cord blood: premature delivery complications, congenital fetal malformations, or any instance of maternal-fetal hemorrhage.¹³⁵ In such situations, the interests of the child in the first moments of life are not advanced by the collection of cord blood for long-term storage. For example, rather than being collected and stored for future use, cord blood may be needed immediately for the emergency resuscitation of a premature neonate. Delays in clamping the umbilical cord may beneficially increase a newborn's blood volume and red blood cell mass, while at the same time decreasing, probably to an unusable amount, the volume of placental and cord blood available for harvesting.¹³⁶

130. See Letter from Dr. Joanne Kurtzberg, Director, Pediatric Bone Marrow Transplant Program, Duke University Medical Center, to the FDA 1 (July 10, 1996) (on file with the FDA).

131. See *id.*

132. See *id.*

133. See *id.*

134. See Cohen, *supra* note 3, at 27-28 (citing literature of ViaCord, one of the nation's largest commercial cord blood banks).

135. See McCullough et al., *supra* note 48, at 614.

136. See Naomi Luban, Director of Transfusion Medicine, Children's National Medical Center, Remarks at the Cord Blood Workshop, *supra* note 27, at 61.

B. *Is Imposition of the IND Mechanism Necessary?*

The scientific rationale for imposing IND requirements upon cord blood storage and transplantation is simple. Because the safest, most effective means of utilizing cord blood, and the long-term safety and efficacy of cord blood transplants are unknown, any use of cord blood products is by definition investigational, and all recipients of cord blood transplants are effectively research subjects entitled to the protections guaranteed by an IND. These protections include qualified investigators, informed consent, institutional review board approval of protocols, and detailed tracking and reporting of clinical outcomes.¹³⁷

By statute, the FDA is charged with assessing the safety and effectiveness of biological products, such as cord blood, that are used to treat diseases in humans.¹³⁸ This oversight requires weighing the risks and benefits inherent in the marketing of any product, and the FDA must base its judgments upon scientific evidence derived from clinical trials.¹³⁹ The scientific method is inherently conservative, and the findings of any one study are only considered valid to the extent that they are replicated, over time and by other investigators.¹⁴⁰ Without sufficient data, therefore, there is no scientific basis for determining *a priori* that a product is safe and effective, even when the results from one or two initial studies appear promising.

Several researchers who provided the FDA with written comments on the first draft regulatory proposal pointed to significant gaps in scientists' knowledge about cord blood transplantation.¹⁴¹ In general, these commentators noted that the field of cord blood transplantation is considered experimental primarily because of its youth. Only about 200 such transplants have been performed, almost all of them in children, and the longest-

137. See generally *supra* notes 71-78 and accompanying text.

138. See sources cited *supra* note 66.

139. See Farley, *supra* note 81, at 31 ("Controlled clinical trials are the only basis, under law, for demonstrating effectiveness.").

140. For a discussion of the scientific method, see generally Bert Black et al., *Science and the Law in the Wake of Daubert: A New Search for Scientific Knowledge*, 72 TEX. L. REV 715 (1994).

141. See, e.g., Letter from Kurtzberg, *supra* note 130, at 1; Letter from Lenfant, *supra* note 41, at 1.

surviving recipients have lived with their transplants for less than ten years.

The risk of potential complications continues throughout a transplant recipient's lifetime,¹⁴² and long-term survival rates are best evaluated by carefully tracking cord blood patients and comparing them to patient groups that have received conventional BMT. The IND regulations generate just this sort of systematic data collection and patient follow-up. The regulations also insure that adverse reactions and bad outcomes are duly reported (underreporting appears to be a problem under current systems of voluntary reporting to patient registries).¹⁴³

The industry's alternative to the FDA's proposal would skip the IND process of clinical investigation and move directly to establishing licensing standards and good manufacturing practices for cord blood. In the view of some researchers, this proposal actually risks hampering the development of the field by prematurely defining standards. Pablo Rubenstein of the New York Blood Center's Placental/Umbilical Cord Program¹⁴⁴ concluded in his comments to the FDA that an IND is a more flexible approach to regulation of a developing field than the codification of strict licensing rules, and that only an IND will ensure "rigorous reporting" of the outcomes of all transplants.¹⁴⁵ Comprehensive outcome information is essential for developing eventual licensing standards; complete risk data are also information that, ethically, transplant patients are entitled to receive.¹⁴⁶ Concurring with this view, the NHLBI, sponsor of the NYBC pilot bank and of the new network of public cord blood banks, stated in a letter to the FDA that its banks plan to comply with IND regulations.¹⁴⁷

142. See generally NCI REPORT, *supra* note 21.

143. See Stephen J. Ackerman, *Watching for Problems that Testing May Have Missed*, FDA CONSUMER, Jan. 1988, at 51, 52.

144. The New York Blood Center is the site of the original NIH-funded pilot program in unrelated donor transplantation. See Cohen, *supra* note 3, at 15-16.

145. See generally Letter from Rubenstein, *supra* note 2, at 1-3 and attachment.

146. See *id.*

147. See Letter from Lenfant, *supra* note 41, at 2.

C. Will the IND Requirement Retard Scientific Progress in the Field of Cord Blood Transplantation?

Virtually without exception, public commentary critical of the FDA's draft regulatory document reflects a similar theme: FDA regulation will retard scientific development in the field of cord blood transplantation. In the FDA's cord blood files are many letters from concerned citizens containing identical language, seemingly generated by advocates of commercial cord blood banking, to the effect that the FDA's approach would "interfere with the ability of trained specialists to practice medicine."¹⁴⁸ Such comments mistakenly associate the viability of commercial blood banking with progress in cord blood transplantation research.

Given the promising results of initial transplantation studies, the number of cord blood research programs is likely to increase, fed by the growing availability of donations through a network of public banks. Qualified physicians conducting transplants under approved protocols will not be prevented from utilizing cord blood under an IND, nor will an IND prevent public or hospital banks from accepting "directed" donations of blood from families who wish to store their newborn's cord blood for the use of a critically-ill family member.¹⁴⁹

It is possible, however, that requiring a period of clinical development would retard the commercialization of cord blood banking, given that insurance companies are unlikely to cover cord blood transplants that would be deemed "experimental" under an IND.¹⁵⁰ Since IND regulations would preclude stor-

148. See, e.g., Letter from Steve and Ruth Gonsoski to the FDA 1 (July 15, 1996) (on file with the FDA).

149. One selling point for private cord blood banks is the opportunity to store directed donations, particularly the cord blood of newborn relatives intended for the use of an ill family member. Directed donations may be important for minority and mixed-race families, whose members are more difficult to match to unrelated donors. The directed donations of at-risk families have been stored and transplanted without the services of private blood banks; for example, the cord blood of a younger relative used to transplant Michael Major, recipient of the first cord blood transplant in the D.C. area, is currently being banked at Children's Hospital in D.C. See Cohen, *supra* note 3, at 12.

150. See *id.*

age facilities from recovering a profit during the IND period of clinical development, it is also possible that facilities that operate solely for the purpose of profiting from the storage of cord blood may not survive.¹⁵¹

Yet, beyond vehement protestations that IND and PLA requirements will hinder advancement of the field, advocates of private cord blood banking offer little evidence that commercialization is critical to cord blood research. Private banks cater to a small number of parents who are affluent (or anxious) enough to purchase storage for a cord blood specimen of dubious value. Meanwhile, the greatest need in cord blood transplantation will be for specimens from unrelated donors.¹⁵² It is even conceivable that a burgeoning private sector banking program might harm cord blood research, if private banks siphon off donations that would otherwise go to the public banks that are participating in clinical trials.

Lastly, it is important to recognize that scientific arguments may mask other considerations in the cord blood controversy. Financial conflicts of interest also cloud the debate between scientists over the appropriateness of FDA regulation. Leading researchers such as Hal Broxmeyer, co-founder of the field of cord blood transplantation, have voiced scientific objections to IND and PLA requirements for cord blood.¹⁵³ Yet, Broxmeyer himself was a founder of the first private cord blood bank, and although he has sold his interest in the company, he reportedly remains a paid industry consultant.¹⁵⁴ Likewise, Paul Billings, the Stanford geneticist and outspoken opponent of IND regulations for cord blood,¹⁵⁵ is also retained as a paid consultant by

151. See *id.* at 15.

152. See Eliot Marshall, *Clinical Promise, Ethical Quandary*, 271 *SCIENCE* 586, 587 (1996).

153. See Letter from Hal Broxmeyer, Indiana University School of Medicine, to the FDA 1 (Apr. 25, 1996) (on file with the FDA).

154. See Cohen, *supra* note 3, at 27-28; see also *id.* at 27, 31 (noting that Biocyte marketing efforts, including the mailing of videos to expectant parents, prompted calls of complaint to FDA).

155. Billings heads the nonprofit affiliate of a private cord blood bank, and he favors adoption of standards developed by industry task force. See Letter from Paul Billings, President, International Cord Blood Foundation, to Cynthia Fisher, President, ViaCord Inc. 1 (July 9, 1996) (on file with the FDA). Billings has sought media attention through a "bioecology" campaign aimed at stopping "cord blood waste." See Cohen, *supra* note 3 at 28.

a private cord blood bank. Perhaps these and other scientists can hardly be criticized for participating in commercial ventures when federal government policies increasingly favor the privatization of scientific research.¹⁵⁶ Nonetheless, fully-informed public debate over cord blood regulation requires disclosure and consideration of scientists' private financial interest, where these interests create the potential for conflict between the ends of public and private gain.

IV. POLICY ISSUES IN PLACENTAL/UMBILICAL CORD BLOOD BANKING

A. *Arguments for Patient Access and Regulatory Reform*

A common fear reflected in parent's letters to the FDA is that regulation of cord blood services will limit patients' access to critical lifesaving therapies, or, at the very least, will deny parents' "right to choose" private cord blood banking.¹⁵⁷ The FDA file contains well over one hundred letters, many with baby photos attached, from parents who often seem to believe that FDA regulations will foreclose the possibility of cord blood storage altogether.¹⁵⁸ These parents' fears are amplified by strident newspaper editorials opposing FDA regulations, which one writer claimed would create "a devastating loss of life."¹⁵⁹

Although cord blood transplantation through approved research programs would remain available to patients, FDA regulations could limit access in one important respect: commercial banks offering nationwide private storage might cease to operate. The absence of an opportunity to bank privately as a form of medical "insurance" is a questionable loss, given that the long-term storage of cord blood, particularly autologous specimens, has no clear medical utility at present. Yet parents who assert a right of access, even to unproved drugs and therapies of uncertain utility, are echoing a sentiment that is at the heart of the FDA reform movement.

156. See generally Bulleit & Bonnet, *supra* note 46.

157. See, e.g., Letter from Gonsoski, *supra* note 148, at 1.

158. See generally Public Comments submitted to the FDA, *supra* note 16.

159. Walter Shapiro, *Don't Limit Patient Access*, USA TODAY, July 12, 1996, at 12A.

Reform advocates in Congress and industry maintain that the FDA fails to adequately consider the hidden costs in lives and suffering to patients who are denied rapid access to new drugs and therapies.¹⁶⁰ To a greater or lesser degree, critics of the FDA urge a shift from current premarket approval requirements to a system of postmarket surveillance in which thresholds to market entry are lowered and products are removed from the market only when sufficient evidence accumulates that a product endangers public health.¹⁶¹

Increased access to new therapies afforded by post-market surveillance and fast-track drug approvals would bring an inescapable increase in the level of risk to consumers. The thalidomide disaster is a paradigmatic example. In the twenty countries where this sedative was placed on the market without an extensive premarket approval procedure, an estimated total of 7,000 to 11,000 limbless babies were born.¹⁶² In the United States, by contrast, the premarket approval process delayed the marketing of thalidomide sufficiently that FDA could avert a large-scale public health crisis.¹⁶³ Similarly, some researchers and AIDS activist groups who successfully lobbied for fast-track approval of new AIDS drugs are now questioning whether it was wise to allow such expensive medications to be "haphazardly tested" and allowed on the market without any clear demonstration of safety and effectiveness.¹⁶⁴

Biologic drugs, vulnerable as they are to contamination, degradation, and unforeseen side effects, will inevitably pose some risk of adverse events regardless of how carefully the drugs are researched and developed. The difference between premarket research and postmarket surveillance, however, is that in clinical trials, participants are informed up front about the experi-

160. See generally C. Frederick Beckner, III, *The FDA's War on Drugs*, 82 GEO. L.J. 529 (1993); see also Walsh & Pyrich, *supra* note 17, at 941.

161. See Beckner, *supra* note 160, at 560.

162. See Morton Mintz, *The Cure That Could Kill You: FDA Reforms Are Bad Medicine*, WASH. POST, July 14, 1996, at C1.

163. See Walsh & Pyrich, *supra* note 17, at 37 ("[T]he FDA was widely praised for not having approved thalidomide for use in the United States.").

164. See Matthew C. Lovell, *Second Thoughts: Do the FDA's Responses to A Fatal Drug Trial and The AIDS Activist Community's Doubts About Early Access to Drugs Hint at a Shift in Basic FDA Policy?* 51 FOOD & DRUG L.J. 273, 277 (1996).

mental nature of the therapy and the full range of risks and benefits involved.

By contrast, once the "experimental" label is removed and a product is released to the market, consumers become unwitting participants in a large-scale clinical trial. In the market, information provided to consumers may be highly asymmetric. Advertising will tout the benefits of a product with little mention of risk, unless the product has been subjected to labeling requirements through FDA drug and biologics regulation. Consumer "choice" in the marketplace of medical care is meaningless if consumers lack sufficient safety information about a therapeutic product, and in the case of cord blood, many of the necessary data about safety and effectiveness have yet to be obtained.

B. *Private Accreditation Versus Government Regulation*

Opponents of FDA regulation argue that the industry should be allowed to police itself, backed up by FDA inspections that would insure compliance with industry standards.¹⁶⁵ The FDA cord blood docket contains various proposals and private accreditation schemes offered by professional societies, by an industry task force, or by individual cord blood banks.¹⁶⁶

To entrust regulatory oversight to the private sector, the FDA must make a policy judgment that the field of cord blood transplantation has matured to the point where commercial ventures are appropriate. In its initial draft document, the FDA cites evidence to the contrary. The agency suggests that the "vigorous commercialization" of cord blood banking, including the patenting of cord blood cryopreservation, has occurred prior to careful consideration of troubling ethical and legal issues. Furthermore, rapid, unregulated commercialization is engendering

165. See generally Public Comments submitted to the FDA, *supra* note 16.

166. See, e.g., Letter from Allen C. Eaves, President, International Society of Hematotherapy and Graft Engineering, to the FDA 1 (Mar. 23, 1996) (on file with the FDA) ("We believe [that the] FDA should accept industry standards for cell processing facilities . . . [and] we recommend that the FDA . . . review facility license applications and conduct compliance inspections. . . .").

unsafe practices and scientifically-insupportable advertising claims.¹⁶⁷

1. Unresolved Bioethics Issues

A hiatus in the commercialization of cord blood services would give researchers, medical ethicists, and policymakers time to consider thorny ethical issues posed by cord blood transplantation. Chief among these are questions of genetic privacy and informed consent.

The medical information that must be collected and linked to a cord blood specimen is extensive, because both the mother and the child must be considered donors. This sensitive compilation of information, which includes a medical history, the mother's sexual history, drug use, and prior travel outside the United States,¹⁶⁸ must be carefully recorded and preserved for the life of the specimen. In the case of cryopreserved cord blood, the life of the specimen is a question that remains to be answered.¹⁶⁹

Additionally, donating mothers must also agree to genetic testing, testing that simultaneously reveals genetic information about the entire family. A medical record containing genetic data poses special privacy concerns, because individuals with known genetic liabilities may encounter difficulties obtaining health insurance or employment.¹⁷⁰ Preserving the privacy of donor identity will be equally important, because transplant recipients who have relapsed may attempt to contact the cord blood donor to request a bone marrow transplant. Some researchers fear that the possibility of such requests might discourage widespread cord blood donation.¹⁷¹

Screening samples for genetic defects and preserving donors' medical privacy are problematic aspects of cord blood donation.

167. See CORD BLOOD DRAFT DOCUMENT, *supra* note 15.

168. See generally McCullough et al., *supra* note 48; see also CORD BLOOD DRAFT DOCUMENT, *supra* note 15.

169. See Cohen, *supra* note 3, at 13.

170. See ASSESSING GENETIC RISKS, *supra* note 40, at 20.

171. See Jerry Sugarman et al., *Ethical Aspects of Banking Placental Blood for Transplantation*, 274 JAMA 1783, 1784 (1995).

The question of what constitutes fully informed consent to cord blood donation is correspondingly complex. Consent procedures may be inadequate unless, prior to giving consent for a donation, parents are informed that they and their baby will be tested, and may receive positive test results, for genetic disorders for which there is no known treatment. Despite uncertainty about what types of genetic tests may one day be developed, cord blood donation agreements must also incorporate a mechanism for obtaining consent for what is called "look-back" testing: future screening of the specimen with tests not yet in existence at the time of donation.¹⁷² In an optimal consent process, parents would be instructed to consider carefully the ramifications of signing a blanket "look-back" authorization that waives all restrictions on the future genetic testing of their child's cord blood.

Conceivably, as an element of informed consent, parents might be told that the practices of testing the newborn's cord blood specimen for genetic disorders—and of retesting the specimen as new genetic tests are devised—violate a key policy recommendation of the nonprofit National Research Council (NRC). In a recent report, the NRC advocated that minors should not be tested for genetic diseases until effective treatments for those diseases become available, due to the psychological and social injuries that may result from positive test findings.¹⁷³ Parents, who serve as surrogates for a child who cannot yet give consent for genetic testing, deserve to be educated about the risks of identifying their child's genetic liabilities. Parents should weigh the social and psychological impact of such information against the small probability that their child will ever benefit from the storage of a cord blood specimen.¹⁷⁴

Voluntary standards that have been devised by the cord blood industry do not adequately address issues of consent and privacy.¹⁷⁵ The FDA's IND process, by contrast, requires in-

172. See *id.* at 1784.

173. See *ASSESSING GENETIC RISKS*, *supra* note 40, at 10.

174. Dr. Paul McCurdy of NHLBI has estimated that the chance of needing a cord blood transplant for leukemia, the most common disease treatable in this manner, at 1 in 200,000. See Cohen, *supra* note 3, at 15.

175. See *id.* at 30.

stitutions that sponsor research to review bioethics concerns through the mechanism of institutional review boards. Thus, to the extent that the FDA ultimately decides not to classify cord blood as an investigatory new drug, ethical issues are likely to be addressed only in an inconsistent, ad hoc fashion.

2. Commodification: "Property" Rights in Cord Blood

To treat cord blood like any other commodity is to open a Pandora's box of property law conundrums. For example, how will ownership rights—including the right to sell a cord blood specimen, to destroy it, to designate it for a particular transplant recipient, or to profit from its use in scientific advances—be divided among infants, parents, physicians, and researchers? To the extent that a market develops, conflicts among potential holders of property interests in cord blood are likely to arise. Parents who decide to discontinue cord blood banking may wish to sell their child's specimen to recoup the costs of collection and storage, rather than continuing to preserve the child's "property" interest in its own cord blood. If parents fall behind in payments, commercial blood banks may assert the right to appropriate and resell banked specimens. Researchers who develop valuable therapies from cord blood may end up competing with donors to capture the resulting profits.¹⁷⁶

Meanwhile, private companies have already asserted intellectual property rights to procedures and techniques involved in cord blood storage and transplantation.¹⁷⁷ At present, it is unclear whether intellectual property protection will, as its proponents argue, stimulate the growth of the cord blood storage industry, or will simply impose a crushing level of royalty expense on nonprofit therapeutic and research users of cord blood.

176. See, e.g., *Moore v. Regents of the University of California*, 793 P.2d 479 (1990), cert. denied, 499 U.S. 936 (1991) (involving suit against physician for conversion of patient's property interests in valuable cell line that physician developed from patient's leukemic spleen cells).

177. See generally Declan Butler, *U.S. Company Comes Under Fire Over Patent on Umbilical Chord Cells*, 382 NATURE 99 (1996).

a. Property Rights in the Body

The traditional, if shopworn, legal metaphor for the concept of property rights is "a bundle of sticks." Each stick in the metaphorical bundle represents a right that the owner has in the property as against other members of society (e.g., a right to sell the property, to destroy it, or to prevent others from using it). To a point, these sticks or rights can be severed from the bundle without destroying the core property interest.¹⁷⁸ With respect to rights in the human body, courts make a clear distinction between two potential sticks in an owner's bundle: (1) the right to control the disposition of a body (or body part); and (2) the right to sell it.¹⁷⁹

Courts have traditionally recognized that individuals and their next-of-kin have a right to determine the disposition of bodies after death.¹⁸⁰ This right falls short of the sort of property interest that would permit the sale of human organs or tissues, because the latter possibility arouses widespread ethical concern, if not moral revulsion.¹⁸¹ The inclusion of disposition, but not commodification interests in the bundle of "property" rights attached to the human body is also a uniform characteristic of state and federal organ donor laws. These laws authorize patients or next-of-kin to designate organs or body parts for transplantation after death, but forbid commercial transactions in the same.¹⁸²

178. For example, an easement to cross a piece of land can be sold without negating the landowner's ownership interest in the underlying real property. *See generally* J.E. Penner, *The "Bundle of Rights" Picture of Property*, 43 UCLA L. REV. 711 (1996).

179. *See infra* notes 180-88 and accompanying text.

180. *See, e.g.,* Brotherton v. Cleveland, 923 F.2d 477 (6th Cir. 1990) (holding that removal of deceased's corneas without permission of next-of-kin is deprivation of constitutionally protected property interest).

181. *See* Moore v. Regents of the University of California, 793 P.2d 479, 497 (1990), *cert. denied*, 499 U.S. 936 (1991) (Arabian, J., concurring) ("Plaintiff has asked us to recognize and enforce a right to sell one's own body tissues *for profit*. He entreats us to regard the human vessel—the single most venerated and protected subject in any civilized society—as equal with the basest commercial commodity. He urges us to commingle the sacred with the profane.") (emphasis in original).

182. *See, e.g.,* National Organ Transplantation Act of 1984, Pub. L. No. 98-507, 98 Stat. 2339 (codified as adopted at 42 U.S.C. §§ 273-74 (1988)); *see generally* Gloria J. Banks, *Legal and Ethical Safeguards: Protection of Society's Most Vulnerable Partici-*

At common law, courts have adopted a similar anti-commodification approach to the living human body. In one important state law case, *Moore v. Regents of the University of California*,¹⁸³ the California Supreme Court concluded, on public policy grounds, that "biological sources" do not possess proprietary rights in their own cells and tissues.¹⁸⁴ The *Moore* court denied the plaintiff, a leukemic patient, a tort action for the conversion of his property interest in a valuable cell line developed from the plaintiff's own diseased spleen cells. The majority concluded that human dignity would be diminished, and medical research chilled, by any commodification of body parts in their "unmodified" (raw) form.¹⁸⁵ To the extent that courts have recognized any type of *antemortem* (before death) ownership interests in cells or tissues (e.g., in frozen sperm, ova, or embryos), the rights recognized have been only quasi-property in nature, usually limited to the right to determine the disposition of a frozen specimen.¹⁸⁶

As a general principle, human organs and tissues, including some human cells under the *Moore* analysis, can be given away, but not sold. Historically, blood has been an exception to this rule.¹⁸⁷ Society has long accommodated a market in blood and blood products without strong ethical objections, perhaps because the human blood supply is replenishable (i.e., it is constantly regenerated by the body)¹⁸⁸ and, thus, blood donation does not deprive the donor of something irreplaceable.

pants in a Commercialized Organ Transplantation System, 21 AM. J.L. & MED. 45 (1995) (reviewing federal and state laws concerning organ donation and transplantation).

183. 793 P.2d 479, *cert. denied*, 499 U.S. 936 (1991).

184. Most courts have skirted property law questions by deeming blood donation to be the provision of a service, not the sale of a good. Thus, blood sales have been exempted from the warranty provisions of the Uniform Commercial Code. The transfer of any property interest in the blood itself blood is regarded as only incidental to this service. See Banks, *supra* note 183, at 49.

185. See *Moore*, 793 P.2d at 492-93 (distinguishing between raw or unmodified human cells, and cultured cells lines, which are the product of human invention).

186. See, e.g., *Davis v. Davis*, 842 S.W.2d 588 (Tenn. 1992) (involving dispute over ownership interests in frozen sperm and fertilized embryos).

187. See *Moore*, 793 P.2d at 489 n.23.

188. See Banks, *supra* note 182, at 47 (explaining the distinction between regenerative and non-regenerative human cells and organs).

The right to sell cord blood cannot be predicated on this distinction, however. Cord blood stem cells are potentially valuable precisely because they are not regenerated within the body of the newborn donor. In this way, cord blood resembles a kidney, an organ for which no legal market exists, more than it does a pint of blood plasma, a commodity that can be bought and sold. Unfortunately, the anti-sale provisions of state and federal organ donation statutes probably do not reach cord blood, given the statutory exceptions for blood and blood products.¹⁸⁹ Without legislative intervention, therefore, there may be few *legal* barriers to the sale of cord blood, unless judges can be convinced that cord blood stem cells, like the leukemic spleen cells in *Moore*, should not be treated as a marketable commodity.

Yet, even if legislators were to grant cord blood the same status as an organ or tissue, by permitting individuals only the right to donate cord blood, ownership of the banked specimen might still be contested. Although genetically, cord blood is the child's blood, the umbilical cord or placenta from which the blood is drawn are tissues that once belonged to the mother's body, as well as, to the child's. If the mother subsequently decides to use stored cord blood for the treatment of her own disease,¹⁹⁰ can her child exercise an ownership veto over this decision? Faced with such a dispute, perhaps a court might conclude that both mother and child share a quasi-property interest in the cord blood specimen.

Alternatively, courts may decide that cord blood is the exclusive property of the newborn infant. An infant lacks the legal capacity to grant consent, either to the medical procedure used to collect the cord blood specimen, or to the disposition of his cord blood through sale or allogenic transplantation. The infant will require a surrogate decision maker, therefore, to make choices about how and when the sample will be used, sold, or destroyed.

189. *See id.*; see also discussion *supra* Part II.E.

190. This is a possibility that is raised in some cord blood marketing literature. *See, e.g.,* United States Cryobanks of Florida, *Umbilical Cord Blood—Frequently Asked Questions* (last modified Jan. 3, 1996) <<http://www.uscryo-cord.com/umbilfaq.html>>.

As guardians of a minor child, parents have the legal capacity to act as surrogate decision makers, yet most courts adhere to the doctrine that parents may only authorize medical procedures that are in the best interests of the child.¹⁹¹ From a property law perspective, parents are also constrained by a fiduciary duty to act in the child's financial best interests and not to profit at the child's expense.¹⁹² Parents' fiduciary obligations and the common-law "best interest" doctrine may give rise to a legal responsibility on the part of parents to preserve cord blood for the benefit of the child donor, rather than using the sample for allogenic transplantation in a sibling or other recipient. The parents who conceive one child in order to obtain cord blood for the benefit of another might, in theory, risk violating a legal obligation to the newborn donor.

Although the absence of case law on cord blood makes the foregoing conclusion speculative, one state court's approach to the somewhat analogous situation of bone marrow donation suggests that parental decisions regarding harvesting and transplantation of their infants' cord blood might be subject to close judicial scrutiny. In *Curran v. Bosze*,¹⁹³ the Illinois Supreme Court faced a wrenching dilemma: the custodial parent of three and one-half year old twins refused to permit the children to be tested as possible bone marrow donors.¹⁹⁴ The potential bone marrow recipient was the twin's half-brother, who required a transplant to treat a rare form of leukemia. The father of all three children sought a court order to compel testing and subsequent bone marrow harvesting, should the twins prove an adequate transplant match for his twelve year old son.¹⁹⁵

In deciding this difficult case, the judge considered two traditional legal standards for surrogate medical decision making. The first standard, advocated by the father, was the doctrine of substituted judgment, which requires a decision maker to establish by "clear and convincing evidence" what decision the pa-

191. See RESTATEMENT (SECOND) OF TRUSTS §2(b) (1957).

192. See W. PAGE KEETON ET AL., PROSSER AND KEATON ON THE LAW OF TORTS § 18, at 115-117 (5th ed. 1984).

193. 566 N.E.2d 1319 (Ill. 1990).

194. See *id.* at 1322.

195. See *id.* at 1321.

tient would make if restored to competency.¹⁹⁶ The alternative standard, proposed by the twins' mother, requires a surrogate medical decision maker to act in the "best interests" of the incompetent patient.¹⁹⁷ The *Curran* court determined that the "substituted judgment" standard was inappropriate when a patient has never been capable of reasoned judgment.¹⁹⁸ In such cases, the court reasoned, a surrogate would have no basis to conclude that if competent, a patient would choose to undergo the procedure.¹⁹⁹ Applying the alternative, "best interests" standard, the court noted the absence of any close relationship between the three children that might result in a psychological benefit to the twins, should the transplant procedure succeed. Weighing the absence of benefit against the identified risks, the court denied the father's request to compel the procedure.²⁰⁰

The *Curran* court did not address whether the twins had any form of property interest in their bone marrow, but the judge's opinion referenced the principles of physical self-determination and "inviolability" upon which the right to refuse medical treatment is founded.²⁰¹ Absent clear evidence of a benefit to the patient, the *Curran* court saw no justification for permitting a parent to abrogate a child's right to bodily integrity.²⁰² In a *Curran*-like dispute over the cord blood, a similar cost-benefit analysis would also require a judge to consider any legally-recognized property interest that newborn has in its own cord blood. Applying a *Curran* approach in the context of cord blood donation, a court might readily second-guess parental decision making, given the potential for conflict between the ultimate interests of newborn donors and their parents.

196. *See id.* at 1325.

197. *See id.* at 1331.

198. *See id.* at 1325.

199. *See id.* at 1326.

200. *See id.* at 1344-45.

201. *See id.* at 1322-26 (citing *In Re Estate of Longeway*, 549 N.E.2d 292 (Ill. 1989)).

202. *See id.* at 1325-26.

b. Intellectual Property Rights in Cord Blood

Although some bioethicists and policymakers remain troubled by the prospect,²⁰³ the Supreme Court has firmly established the viability of intellectual property rights in living cells, tissues, and organisms created through human invention.²⁰⁴ In *Diamond v. Chakrabarty*,²⁰⁵ the Court held that a genetically engineered bacterium used to degrade crude oil fell within the scope of the federal patent statute.²⁰⁶ This statute permits patents for, *inter alia*, "the manufacture or composition of matter"²⁰⁷ Federal patent protection has subsequently been extended to human cell lines and to entire animals whose genetic composition has been modified.²⁰⁸ Inventors may also obtain patents for processes or machines used in the handling or storage of living organisms, so long as the subject of the patent is novel, useful, and non-obvious to someone skilled in the relevant art.²⁰⁹

Under the prevailing legal standard for patentable subject matter, a United States corporation, Biocyte, was granted a patent in 1993 covering "hematopoietic stem and progenitor cells of neonatal or fetal blood, that are cryopreserved, and the therapeutic uses of such stems and progenitor cells upon thawing."²¹⁰ In 1996, Biocyte obtained similar patent protection in Europe.²¹¹ The validity of these cord blood patents—which, if

203. See generally Mark Crawford, *Religious Groups Join Animal Patent Battle*, 237 SCIENCE 480 (1987).

204. See generally Leon R. Kass, *Patenting Life*, 63 J. PAT. & TRADEMARK OFF. SOC'Y 571 (1981); Thomas Moga, *Transgenic Animals as Intellectual Property (or the Patented Mouse That Roared)*, 76 J. PAT. & TRADEMARK OFF. SOC'Y 511 (1994).

205. 447 U.S. 303 (1980).

206. See *id.* at 318.

207. 35 U.S.C. § 101 (1994).

208. In 1988, the United States Patent and Trademark Office issued its first animal patent for a genetically-altered mouse developed at Harvard University. See U.S. PATENT NO. 4,736,866.

209. See generally 35 U.S.C. §§ 100-04 (1994).

210. Butler, *supra* note 177, at 99.

211. See David Rowan, *Analysis Money in Genes: Signing up to "A Patent on Life"; Britain Agrees Today to an EU Directive that Could Mean that the Ownership of Your Blood Cells and Your Genes Could be Transferred to a Company that Holds the Patents. What's Going On?*, THE GUARDIAN, Nov. 27, 1997, available in 1997 WL 14743278; *Transplantation Groups Say European Blood Cell Patent Unethical*, CANCER WEEKLY PLUS, Mar. 3, 1997, available in 1997 WL 6219335.

upheld, will require all users of cord blood to pay royalties to Biocyte—is currently the subject of legal challenges in the United States and Europe.²¹²

Researchers fear that patent rights to the exclusive use of cryogenic techniques for cord blood storage and transplantation will make nonprofit cord blood research prohibitively expensive, by forcing users of cord blood to pay costly royalties or to defend against infringement actions.²¹³ European scientists have been particularly outspoken in their objection to the Biocyte patents, citing prohibitions against for-profit organ donation in a resolution of the International Society of Transplantation. For instance, Eliane Gluckman, head of the European research team that performed one of the first allogenic cord blood transplant operations, has urged on behalf of a consortium of European researchers that donations of human cells in any form should be “free and anonymous” as a matter of public policy.²¹⁴

Such ethical objections will have little bearing on the ultimate validity of the Biocyte patents in the United States.²¹⁵ Instead, the legal process for re-examining the patent will focus upon a narrow question: is there evidence in the scientific literature or elsewhere that the Biocyte process for storing cord blood in liquid nitrogen was contemplated by others prior to the dates on which the company filed its patent applications, contradicting the company's claims of novelty and non-obviousness?²¹⁶ Absent evidence to the contrary, public policy arguments against the patenting of human cells and related therapies are unlikely to persuade the reviewing court. The Supreme Court has stated clearly that Congress must define the ethical limits of patentable subject matter, because the issue is “a

212. See Pete Mitchell, *European Researchers Condemn U.S. Firm's Cord-Blood-Storage Patent*, 349 THE LANCET 1232 (1997).

213. See *id.* at 1232-33.

214. See *id.*

215. The European patent process does contain a mechanism for challenging patents where the patent grant is contrary to public order or morality. See generally ARTICLE 53, EPC CONVENTION ON THE GRANT OF EUROPEAN PATENTS, 5 October 1973, as amended 17 December 1991 and by the decisions of the Administrative Council of the European Patent Organization of 21 December 1978, 13 December 1994, 20 October 1995, and 5 December 1996.

216. See Butler, *supra* note 177, at 99.

matter of high policy for resolution within the legislative process after the kind of investigation, examination, and study that legislative bodies can provide, and courts cannot."²¹⁷

3. Unsafe Practices

A number of researchers have written to the FDA or have otherwise expressed their concern that unregulated cord blood banking activity poses a threat to the public health.²¹⁸ Concerns cited include unsafe practices in the harvesting, transportation, and storage of cord blood.

In an apparent attempt to avoid creating the regulatory trigger of a nexus to interstate commerce, some private cord blood banks request that parents ship specimens to the bank via express mail, a system that provides no form of temperature control or protection against contamination.²¹⁹ One physician has complained to the FDA that the collection "kit" provided to his expectant patient was wholly unsuited for the transportation of blood and consisted of a "grossly inadequate" packaging material likely to leak blood products.²²⁰ Another letter expressed concern that some cord blood specimens have been preserved in fetal calf serum, raising serious viral transmission issues.²²¹

Cord blood storage and transplantation practices have also been the subject of criticism. According to one leading researcher, some blood banks fail to test whether the cells that they store remain viable and free from contamination.²²² There are concerns that patient identifying information is not being adequately maintained and tracked and that cord blood transplants are being performed by persons with little experience in stem cell transplantation.²²³ A particular danger is that transplants

217. *Diamond v. Chakrabarty*, 447 U.S. 303, 317 (1980).

218. See generally Public Comments submitted to the FDA, *supra* note 16.

219. See Letter from Kutzburg, *supra* note 130, at 1.

220. See Letter from Robert J. Carpenter, M.D., Associate Professor of Obstetrics and Gynecology, University of Texas Medical School, to the FDA 1 (Aug. 21, 1996) (on file with the FDA).

221. See Letter from Howe, *supra* note 118, at 1.

222. See Letter from John E. Wagner, Director, International Cord Blood Transplant Registry, to the FDA 1 (July 26, 1996) (on file with the FDA).

223. See Letter from Kutzburg, *supra* note 130, at 1; see also Letter from Carpen-

are being performed without proper antigen typing, resulting in dangerous HLA antigen mismatches that increase the likelihood of graft-versus-host disease.²²⁴

4. Truth in Advertising

Manipulative promotional schemes and unsubstantiated claims about the therapeutic utility of cord blood have been the source of repeated complaints to the FDA.²²⁵ One of the more controversial marketing practices in commercial cord blood banking is the mailing of unsolicited promotional videos to expectant parents. The content of such materials, which exhort parents to make the "potentially lifesaving" decision to store their infant's cord blood, for fees typically amounting to more than \$1,000 plus additional yearly charges,²²⁶ exploits parents' most basic fears for the health of a newborn child.²²⁷

Most troublesome from a regulatory standpoint are the highly misleading claims common to much cord blood advertising material. Promotions portray cord blood transplants, not as an experimental medical procedure, but as a routine alternative to BMT.²²⁸ The literature typically does not distinguish between autologous donations, which may be useless, and allogenic donations.²²⁹ Additionally, while obscuring the rarity of the potential need for a cord blood transplant, these advertisements imply that cord blood can or soon will be used to cure everything from AIDs to cancer. In one particularly egregious example, a cord blood bank in the state of Florida offers promotional materials on the World Wide Web that cite the "one in eight" risk of breast cancer among women in the United States and

ter, *supra* note 220, at 1; Wagner, *supra* note 222, at 1.

224. See Letter from John F. DiPersio, Chief, Division of Bone Marrow Transplantation and Stem Cell Biology, Washington University School of Medicine, to the FDA 1 (Mar. 22, 1996) (on file with the FDA); see also Wagner, *supra* note 222, at 1.

225. See Telephone Interview with Harvath, *supra* note 14.

226. See Cohen, *supra* note 3, at 11.

227. Viacord Inc., one of the largest private banks in Boston, charges \$1,500 to harvest cord blood, and an additional \$95 per year to store the specimen. See Claudia Kalb & Melinda Beck, *Seizing Nature's Lifeline*, NEWSWEEK, Apr. 29, 1996, at 75.

228. See *Parents Fear Rules*, *supra* note 16, at A2.

229. See *id.*

suggest that in light of this risk, "storing cord blood makes sense as a source of stem cells for the mother. . . ." ²³⁰

Even if gene therapy for breast cancer did exist, there is no evidence that cord blood stored today could ever be used for such treatment. Indeed, no one knows if cord blood stem cells that have been frozen for more than a few years even remain viable. Yet, without full regulatory oversight of the cord blood industry, the FDA will be unable to invoke the FFDCA's advertising and labeling provisions, which the agency uses to protect consumers by requiring that drug promotional materials present a balanced view of effectiveness claims and risk information.²³¹ As the CEO of a medical device company has noted, a primary effect of IND/PLA regulations is to impose a "truth in advertising" mandate upon the medical products industry.²³²

In addition, the FDA has just begun to consider the problems posed by Internet advertisements.²³³ A considerable amount of misleading and erroneous information about medical products is available on World Wide Web pages, and cord blood is no exception. IND regulations prohibit advertisements of the safety and effectiveness of an experimental drug, but safety and effectiveness data are often available on the Internet in the form of communications between researchers, or in information provided by a company to shareholders.²³⁴ Such information is also accessible to patients, and can become distorted as preliminary findings are disseminated among patient advocacy newsgroups.²³⁵ Although the FDA is concerned by marketing efforts directed at the public via web pages,²³⁶ the agency can only influence the content of advertising for the products that it regulates.

230. United States Cryobanks of Florida, *Umbilical Cord Blood—Frequently Asked Questions* (last modified Jan. 3, 1996) <<http://www.uscryo-cord.com/umbilfaq.html>>.

231. See discussion *supra* Parts II.D.1-3.

232. See Letter from Philip H. Coelho, President and CEO, ThermoGenesis Corp., to the FDA 1 (July 1, 1996) (on file with the FDA).

233. See Peter S. Reichertz, *Legal Issues Concerning the Promotion of Pharmaceutical Products on the Internet to Consumers*, 51 FOOD & DRUG L.J. 355, 356-61 (1996).

234. See Promotion of FDA-Regulated Medical Products on the Internet; Notice of Public Meeting, 61 Fed. Reg. 48,707-09 (1996).

235. See *id.*

236. See *id.*

C. "Back Door" Regulating and the Reach of the FFDCA

In briefs submitted during the public comment period for the first draft document on cord blood,²³⁷ some industry officials objected that the FDA was exceeding its regulatory mandate.²³⁸ These industry documents raised both substantive and procedural issues under administrative law. Chief among the procedural objections is the claim that the FDA, by labeling its document a *draft document*, while at the same time inviting the submission of INDs for clinical trials, is "threatening" the industry into compliance while evading the more complex process of rulemaking.²³⁹

Rulemaking, including a period of "notice and comment," is required under section 553(b) of the Administrative Procedure Act whenever an agency creates substantive rules, as opposed to issuing statements of policy.²⁴⁰ Notice and comment rulemaking requires economic and cost-benefit analyses,²⁴¹ paperwork reduction analyses,²⁴² analyses of the impact of the proposed regulation on small businesses,²⁴³ and, with the passage of the Congressional Review Act of 1996, imposes delays caused by mandatory Congressional review of most new FDA rules.²⁴⁴

The FDA describes a draft document as an "informal communication."²⁴⁵ Such a document sets out, in the "best judgment of FDA employees at this time," the agency's proposed approach

237. The public comment period was extended for three months at industry request.

238. See Letter (Petition for Stay of Administrative Action) from Kathleen M. Sanzo, Morgan Lewis & Bockius, to the FDA 28 (June 6, 1996) (on file with the FDA).

239. See *id.*

240. 5 U.S.C. § 553(b) (1994).

241. See Exec. Order No. 12,866, 58 Fed. Reg. 51,735 (1993), reprinted in 5 U.S.C. § 601 (1994) (requiring cost-benefit analyses of regulatory alternatives).

242. See Paperwork Reduction Act of 1995, 13 U.S.C. § 91; 44 U.S.C. §§ 3501-20 (Supp. I 1995).

243. See Regulatory Flexibility Act, 5 U.S.C. §§ 601-12 (1994).

244. 5 U.S.C. Sec. 801(a)(3) (1994). For a full discussion of the impact of this legislation, see generally James T. O'Reilly, *FDA Rulemaking After the 104th Congress: Major Rules Enter the Twilight Zone of Review*, 51 FOOD & DRUG L.J. 677 (1977).

245. See Food and Drug Administration regulations, guidelines, recommendations, and agreements, 21 C.F.R. §10.90(b)(9) (1997).

to regulation of a new product.²⁴⁶ Informal communications under the Code of Federal Regulations are not binding on the agency, nor do they necessarily represent what will be the content of a formally proposed rule.²⁴⁷ The stated purpose of the cord blood draft documents is to elicit comments during the development of a proposed rule. One ancillary purpose, however, may be to dampen rampant commercialization of cord blood services by placing entrepreneurs on notice that the agency intends to assert some form of regulatory oversight.

The principal substantive legal objection to the FDA proposal is the argument that the agency cannot justifiably require an IND for cord blood.²⁴⁸ The author of one industry brief asserts that cord blood collection cannot be considered a clinical investigation under the IND regulations of the FFDCA, because no drug is being "administered or dispensed," and no "clinical investigators" are involved.²⁴⁹ Resolution of this point turns on the extent of the FDA's latitude to define the category of experimental new drugs. If cord blood can validly be considered a new drug, then IND regulations are consistent with this classification.

Although the FDA cannot classify products in an "arbitrary and capricious" manner without violating the Administrative Procedure Act,²⁵⁰ precedent suggests that the agency has broad discretion to define new products as regulable drugs, devices, or biologics.²⁵¹ The actual limits of the agency's discretion will likely be clarified by litigation over the FDA's new tobacco advertising regulations, as the tobacco industry challenges the FDA's assertion of jurisdiction over cigarettes as medical devices.²⁵²

246. See CORD BLOOD DRAFT DOCUMENT, *supra* note 15, at 1.

247. Whether or not a communication issued as a draft document under 21 C.F.R. 10.90(b)(9) represents a thinly-veiled attempt to impose binding rules is an issue beyond the scope of this paper.

248. See generally Public Comments submitted to the FDA, *supra* note 16.

249. Letter from Sanzo, *supra* note 238, at 28-29 (citing Investigational New Drug Application: Definitions and Interpretations, 21 C.F.R. § 312.3(b) (1997)).

250. See 5 U.S.C. § 706(2)(a) (1994).

251. See *supra* note 69 and accompanying text.

252. See FDA Tobacco Regulations, *supra* note 66.

V. THE HUMAN TISSUES SAFETY ACT OF 1996 (TISSUE ACT)

This bill, sponsored by Senator Wyden of Oregon and cosponsored by Senators Dodd and Simon, would preempt FDA regulation of cord blood and human tissues.²⁵³ The bill revokes the FDA's proposed regulations for the transplantation of tissues,²⁵⁴ substituting only minimal requirements to govern tissue facility registration, operation, and advertising.²⁵⁵ Specifically exempted from the bill are organs, gene therapy, and blood products, thus preserving existing regulatory oversight in these areas. But in a seemingly inconsistent provision of the bill, cord blood is singled out and expressly defined as a tissue, the use of which is broadly deregulated.²⁵⁶

The Tissue Act defines human tissue, and cord blood, as a "collection of similar human cells" that is "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease or condition in a human or for reproduction" and that "achieves its primary intended purpose through repair or replacement of bodily tissue through structural support or cellular function."²⁵⁷ According to the bill's text, the FDA may not reclassify human tissue as a drug, a biologic, or a medical device, (thereby subjecting tissues to a regulatory scheme) unless the following conditions are met: (1) users of the tissue in question have been required to collect retrospective data or to maintain a patient registry for at least five years; and (2) "insufficient data exist to confirm the safety and clinical benefit from the use of such tissue."²⁵⁸ Alternatively, reclassification may occur if use of the particular tissue product presents an "immediate hazard to public health."²⁵⁹ The registry requirement that is a prerequisite to reclassification of a tissue may only be imposed

253. See S. 2195, 104th Cong. (1996) [hereinafter Tissue Act]. The legislation, entitled "A Bill to Provide to for the Regulation of Human Tissue for Transplantation to Ensure That Such Tissue is Handled in a Manner to Preserve its Safety and Purity," was introduced in the Senate on October 3, 1996. The bill was subsequently referred to Committee on Labor and Human Resources.

254. See CELLULAR & TISSUE BASED PRODUCTS, *supra* note 20.

255. See Tissue Act, *supra* note 253, at § 352A.

256. See *id.* at § 352A(i).

257. See *id.* at §§ 1(a)(hh)(1)(A)-(B).

258. See *id.* at § 352A(f)(1)(A).

259. See *id.* at § 352A(f)(1)(B).

once the FDA has engaged in the lengthy process of notice and public comment.²⁶⁰

As he introduced the bill, Senator Wyden offered the following rationale for legislative intervention: historically, the use of allogenic (donor) tissue has not been subject to premarket approval; therefore, it makes no sense to subject autologous (a patient's own) tissue to heightened regulation.²⁶¹ Wyden also opined that the FDA's premarket approval process was designed only for "synthetic" compounds with unpredictable effects.²⁶² In his comments on the Senate floor, Senator Wyden concluded:

This bill also recognizes that human cells and tissues are not drugs, biological products, or medical devices, and that it is inappropriate to regulate them as if they were. Drugs may be toxic or carcinogenic, while tissue is not. Drugs circulate in the bloodstream and have systemic effects, while tissue is typically transplanted into a localized area and does not circulate in the blood. For these, and many other reasons, tissue is generally less risky than the products that FDA traditionally regulates.²⁶³

Such sweeping generalizations about the safety of tissue transplantation seem at best misguided, particularly with respect to novel tissue manipulation and transplantation procedures for which few clinical data, and virtually no long-term outcome data, exist. The fact that bone marrow transplantation predated comprehensive FDA regulation of tissues is a red herring with little relevance to the question of whether novel techniques such as cord blood transplantation should be exempted from regulatory oversight.

Nor is it correct to assume, as do the supporters of the Tissue Act, that tissue transplantation is inherently less risky than the administration of a drug. Blood "tissues" in particular may produce lethal immunological reactions when transplanted. Blood tissues may also be "carcinogenic," in the sense that the transplantation of blood stem cells carries the risk of transmit-

260. *See id.*

261. *See* 142 CONG. REC. 512309 (daily ed. Oct. 3, 1996) (statement of Sen. Wyden).

262. *See id.*

263. *Id.*

ting genetic predispositions to cancer, in addition to the direct transmission of infectious disease. Furthermore, these risks may be higher—and not lower as Senator Wyden's comments imply—if a cancer patient's autologous cord blood is used for transplantation.

Risks of cancer and toxicity do not arise solely from products that "circulate within the blood," as the Tissue Act seems to imply. In the case of stem cell transplantation, this systemic/nonsystemic distinction is meaningless; stem cells must migrate through the bloodstream to their ultimate transplantation "site," the bone marrow.²⁶⁴ Once engrafted, stem cells discharge their progeny, blood cells, directly into the circulatory system. Thus, even if organs and cartilage could be distinguished from drugs because the former are tissues "transplanted into a localized area,"²⁶⁵ this distinction would still not provide a basis for excluding cord blood transplantation from the FDA's IND regulations.

VI. CONCLUSION

The federal government has not been slow to appreciate the potential of placental and umbilical cord blood transplantation. As Paul Coelho, president and CEO of Thermogenesis (a medical device company) noted in his comments on the first draft proposal for the regulation of cord blood, "the FDA has moved very rapidly to assist the development of this therapy in the United States, the only country where a comprehensive cord blood program is already in place (supported by NIH funding), is already saving lives, and soon may be generally available to all patients."²⁶⁶ The NIH-funded network of public cord blood banks represents a large scale government investment, more than thirty million dollars, in cord blood research and development.²⁶⁷ Through this public banking network, allogenic trans-

264. See CELLULAR & TISSUE-BASED PRODUCTS, *supra* note 20, at Part V.B(2)(d). Hematopoietic stem cells have a metabolic (systemic) mode of action, and the failure or improper functioning of such cells can create adverse, life-threatening systemic events. See *id.*

265. Statement of Senator Wyden, *supra* note 261.

266. Letter from Coelho, *supra* note 232, at 1.

267. See Cohen, *supra* note 3, at 13.

plantation will be available to a far wider number of patients than those few who can afford, or might ever face the need, to store their infant's blood privately.

In the interests of sound science and consumer protection, the FDA should reaffirm its initial decision to treat cord blood as an investigatory new drug, subject to a period of clinical development. The NHLBI, sponsor of this public system, supports the FDA's proposed IND regulation of cord blood and is fully prepared to comply with IND requirements. NHLBI Director Claude Lenfant emphasizes that the IND mechanism "is wholly consistent with conducting responsible research"²⁶⁸ Lenfant adds: "Since research in general operates with protocols, data collection, and data analysis, an IND requirement will neither impose an undue burden nor constitute an inhibitory influence on research."²⁶⁹

The FDA's partial retreat from an initial position that commercialization should follow science in cord blood transplantation is troubling. The agency's revised plan to exempt autologous uses of cord blood from an IND seems illogical, given that autologous uses have been the subject of far less research than allogenic uses. Furthermore, most of the unresolved questions about safe collection, storage, and transplantation protocols apply equally to all procedures involving cord blood, regardless of the identity of the transplant recipient.

Nonetheless, a watered-down version of IND regulation is still preferable to legislation such as the Tissue Act. Even those who disfavor the imposition of any premarket approval requirements generally agree that cord blood deserves a level of oversight consistent with the FDA's recently-heightened regulation of blood donation facilities.²⁷⁰ Yet, by effectively removing cord blood from FDA jurisdiction pending a public health crisis, the Tissue Act legislation is a far more drastically deregulatory approach than even the one favored by the cord blood industry.

268. Letter from Lenfant, *supra* note 41, at 1.

269. *Id.*

270. These regulations include establishment licensure (ELAs), requirements to adhere to good manufacturing practice guidelines (GMPs), FDA inspection and sanctions for non-compliance, and mandatory patient tracking and data reporting. See *supra* notes 144-47 and accompanying text.

Essentially, under the Tissue Act, the resolution of all outstanding issues in cord blood transplantation—from privacy and consent to appropriate manufacturing protocols—would be left to the vagaries of the private market. Consumers are ill-served by this type of “regulatory reform,” in which legislators substitute their own judgment for that of scientific experts and the public health is staked on a roll of the free market dice.²⁷¹

271. Subsequent to the completion of this article, the Working Group on Ethical Issues in Umbilical Cord Blood Banking published a consensus statement in the *Journal of the American Medical Association*. See Jeremy Sugarman et al., *Ethical Issues in Umbilical Cord Blood Banking*, 278 JAMA 938 (1997). The multidisciplinary group of experts in blood banking, bone marrow transplantation, obstetrics, ethics, law, and social sciences concluded that, given the uncertain and exploratory nature of the science of umbilical stem cell (UBC) transplantation, “UBC banking and use ought to be considered an investigational technology rather than a proven treatment.” *Id.* at 942. The group expressed reservations about the FDA’s modified regulatory proposals and cautioned further that “[b]ecause of the current paucity of scientific data to support the future use of autologous stem cells,” stem cell banking for autologous uses is at best “speculative.” *Id.* The group noted that current marketing of commercial UBC services is characterized by statements that tend to mislead parents about the necessity or utility of UBC banking. See *id.* at 242-43.